

In the claims:

Please cancel claims 12-16, 18-22, 37, 44, and 45.

Please amend claims 9, 10, 17, 28, 39-43, and 46.

Please add new claims 47-62.

1-5. **(Canceled)**

6. **(Previously presented)** The recombinant inhibitor protein of claim 39, wherein the kallikrein is hK2 kallikrein.

7. **(Canceled)**

8. **(Canceled)**

9. **(Currently amended)** The recombinant inhibitor protein of any one of claims 39, 40, 41, 43, or 47, wherein the serpin sequence is selected from the group consisting of  $\alpha$ -1 antichymotrypsin (ACT), protein C inhibitor (PCI),  $\alpha$ -1 antiprotease (AAT), human  $\alpha$ -1 antitrypsin-related protein precursor (ATR),  $\alpha$ -2-plasmin inhibitor (AAP), human anti-thrombin-III precursor (ATIII), protease inhibitor 10 (PI10), human collagen-binding protein 2 precursor (CBP2), protease inhibitor 7 (PI7), protease inhibitor leuserpin 2 (HLS2), human plasma protease C1 inhibitor (C1 INH), monocyte/neutrophil elastase inhibitor (M/NEI), plasminogen activator inhibitor-3 (PAI3), protease inhibitor 4 (PI4), protease inhibitor 5 (PI5), protease inhibitor 12 (PI12), human plasminogen activator inhibitor-1 precursor endothelial (PAI-1), human plasminogen activator inhibitor-2 placental (PAI2), human pigment epithelium-derived factor precursor (PEDF), protease inhibitor 6 (PI6), protease inhibitor 8 (PI8), protease inhibitor 9 (PI9), human squamous cell carcinoma antigen 1 (SCCA-1), human squamous cell carcinoma antigen 2 (SCCA-2), T4-binding globulin (TBG), Megsin, and protease inhibitor 14 (PI14).

10. **(Currently amended)** The recombinant inhibitor protein of claim 39, wherein said recombinant inhibitor protein is selected from the group consisting of SEQ ID NO: 2, SEQ

ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, and SEQ ID NO: 14, MD820, MD 62, MD 61, MD 67, and MDCL.

11-16. **(Canceled)**

17. **(Currently amended)** A pharmaceutical composition comprising the recombinant inhibitor protein of claim 39 or 40, and a pharmaceutically acceptable carriers.

18-27. **(Canceled)**

28. **(Currently amended)** A method for producing the recombinant inhibitor protein of claim 39, comprising

- a) selecting a polynucleotidic sequence encoding a substrate active site ~~specific for~~ which inhibits said Kallikrein;
- b) introducing said polynucleotidic sequence into a sequence encoding a serpin, so as to obtain a recombinant inhibitor protein;
- c) allowing expression of said recombinant inhibitor protein in a cell expression system under suitable conditions; and
- d) recovering said recombinant inhibitor protein.

29. **(Previously presented)** The method of claim 28, wherein step a) is performed by phage-displayed library screening.

30. **(Previously presented)** The method of claim 28, wherein the suitable conditions comprise culturing the cell expression system at a temperature between 10-40°C during 10-30 hours.

31. **(Previously presented)** The method of claim 30, wherein the suitable conditions comprise a temperature of 16°C during 16 hours.

32. **(Previously presented)** The method of claims 28, wherein step d) is achieved by separation after extraction of said recombinant inhibitor protein from the cell expression system.

33. **(Previously presented)** The method of claim 32, wherein the separation of said recombinant inhibitor protein is achieved by affinity chromatography.
34. **(Previously presented)** The method of claim 28, wherein the recombinant inhibitor protein is further assayed for its ability to inhibit the activity of said kallikrein.
35. **(Canceled)**
36. **(Previously presented)** The method of claim 28, wherein the cell expression system is a bacterial cell.
37. **(Canceled)**
38. **(Previously presented)** A diagnostic kit for the detection of a kallikrein in a specimen comprising the recombinant inhibitor protein of claim 39.
39. **(Currently amended)** A recombinant inhibitor protein, or an inhibiting fragment thereof, which inhibits specific for a kallikrein, comprising a serpin sequence comprising a modified Reactive Serpin Loop (RSL) having a substituted P1-P1' scissile bond-containing pentapeptide, wherein P1 is an arginine (R) or a lysine (K) ~~the modified RSL is modified by at least one additional substrate active site sequence resulting~~ which results in increased binding affinity for said kallikrein.
40. **(Currently amended)** A recombinant inhibitor protein, or an inhibiting fragment thereof, ~~specific for~~ which inhibits a kallikrein hK2, comprising a serpin sequence comprising a modified Reactive Serpin Loop (RSL) having a substituted P1-P1' scissile bond-containing pentapeptide ~~wherein the modified RSL is modified by at least one substrate active site sequence resulting~~ which results in increased binding affinity for said kallikrein hK2.
41. **(Currently amended)** A recombinant inhibitor protein which inhibits a kallikrein, or ~~an~~ a kallikrein inhibiting fragment thereof, ~~specific for a kallikrein~~, comprising a serpin sequence comprising a modified Reactive Serpin Loop (RSL), wherein the amino acid sequence

of the modified RSL is selected from the group consisting of SEQ ID No 16, 17, 18, 19, 20, 21, and 22.

42. **(Currently amended)** The recombinant inhibitor protein of claim 39, wherein the pentapeptide at least one substrate active site sequence specific for said kallikrein is a substrate peptide selected by said kallikrein using a phage-displayed random pentapeptide library.

43. **(Currently amended)** A recombinant inhibitor protein, or an inhibiting fragment thereof, specific for a kallikrein, which inhibits a kallikrein, comprising a serpin sequence comprising a modified Reactive Serpin Loop (RSL), wherein a P6 – P6' ~~region~~ of the RSL comprises an arginine (R) or a lysine (K) at P1 and is modified by at least one additional substrate active site sequence.

44-45. **(Canceled)**

46. **(Currently amended)** The recombinant inhibitor protein of claim 43, wherein the a P3-P3' region of the RSL is modified by at least one additional substrate active site sequence is modified in P3-P3'.

47. **(New)** A recombinant inhibitor protein, or an inhibiting fragment thereof, which inhibits a kallikrein, comprising a serpin sequence comprising a modified Reactive Serpin Loop (RSL), wherein the modified RSL comprises arginine (R) or lysine (K) at P1, and comprises at least one additional modified substrate active site sequence within P5 to P'4, which results in increased binding affinity for said kallikrein.

48. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P'1 is selected from the group consisting of alanine, methionine, proline, leucine, phenylalanine, isoleucine, aspartic acid, and glutamine.

49. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P'1 is selected from the group consisting of threonine, serine, and valine

50. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P3 – P'2 of the RSL is modified by at least one substrate active site sequence.

51. **(New)** The recombinant inhibitor protein of claim 50, wherein P3 – P'2 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 58, and SEQ ID NO: 67.

52. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P4 – P'1 of the RSL is modified by at least one substrate active site sequence.

53. **(New)** The recombinant inhibitor protein of claim 52, wherein P4 – P'1 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 35, SEQ ID NO: 42, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 57, SEQ ID NO: 62, SEQ ID NO: 63, and SEQ ID NO: 66.

54. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P2 – P'3 of the RSL is modified by at least one substrate active site sequence.

55. **(New)** The recombinant inhibitor protein of claim 54, wherein P2 – P'3 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 31, SEQ ID NO: 43, SEQ ID NO: 46, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 55, SEQ ID NO: 60, SEQ ID NO: 61, and SEQ ID NO: 68.

56. **(New)** The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P1 – P'4 of the RSL is modified by at least one substrate active site sequence.

57.     **(New)**           The recombinant inhibitor protein of claim 56, wherein P1 – P'4 comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 34, SEQ ID NO: 38, SEQ ID NO: 48, SEQ ID NO: 54, and SEQ ID NO: 59.
58.     **(New)**           The recombinant inhibitor protein of any one of claims 39, 43, or 47, wherein P5 – P1 of the RSL is modified by at least one substrate active site sequence.
59.     **(New)**           The recombinant inhibitor protein of claim 58, wherein P5 – P1 comprises an amino acid sequence set forth in SEQ ID NO: 65.
60.     **(New)**           The recombinant inhibitor protein of claim 39 or 40, comprising at least two additional substrate active site modifications.
61.     **(New)**           The recombinant inhibitor protein of claim 39 or 40, comprising at least three additional substrate active site modifications.
62.     **(New)**           An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO 16, 17, 18, 19, 20, 21, and 22.